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EXAMINER

ALONZO, NORMA LYN

ART UNIT	PAPER NUMBER
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1632

DATE MAILED: 09/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/663,454

Applicant(s)

MURRAY ET AL.

Examiner

Norma C Alonzo

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
 - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
 - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
 - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 7/1/04.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-21 is/are pending in the application.
- 4a) Of the above claim(s) 9-12 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-8 and 13-21 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 15 September 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 1/27/04 & 6/14/04.
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of group I, claims 1-8, 13-21, drawn to a transgenic non-human animal and a method for making said animal, in the reply filed on July 1, 2004 is acknowledged.
2. Claims 9-12 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 7/1/04.
3. Claims 1-8 and 13-21 are under consideration.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-8 and 13-21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a transgenic mouse and transgenic goat whose somatic and germ cells comprise a nucleic acid sequence encoding stearyl-

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CoA desaturase (SCD) operably linked to a mammary gland specific promoter wherein said transgene is expressed in the mammary gland of said mouse and goat and wherein milk of said mouse and said goat contains said SCD transgene, a method for harvesting or processing said milk, and a method of producing said mouse and said goat wherein stearoyl-CoA desaturase transgene is microinjected into a single celled mouse or goat embryo wherein mouse or goat embryo is transferred into a mouse or goat female, does not reasonably provide enablement for

- 1) any transgenic non-human mammal other than mouse or goat
- 2) comprising a transgene encoding any fatty acid desaturase
- 3) wherein said transgene comprises a coding sequence for a SCD operably linked to any animal tissue specific promoter other than mammary gland tissue promoter
- 4) a method for producing said transgenic non-human animal comprising introducing a desaturase transgene into a somatic cell, forming a genetically modified somatic cell comprising a genetically modified nucleus and transferring said genetically modified somatic cell into a single celled embryo, transferring the genetically modified embryo into a recipient female wherein the genetically modified embryo develops into a transgenic animal
- 5) and a method for producing a food product comprising harvesting or processing a food product from said transgenic non-human animal.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims as discussed below.

While determining whether a specification is enabling, one considers whether the claimed invention provides sufficient guidance to make and use the claimed invention, if not, whether an artisan would have required undue experimentation to make and use the claimed invention and whether working examples have been provided. When determining whether a specification meets the enablement requirements, some of the factors that need to be analyzed are: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples, and whether the quantity of any necessary experimentation to make or use the invention based on the content of the disclosure is "undue" (*In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). Furthermore, USPTO does not have laboratory facilities to test if an invention will function as claimed when working examples are not disclosed in the specification, therefore, enablement issues are raised and discussed based on the state of knowledge pertinent to an art at the time of the invention, therefore skepticism raised in the enablement rejections are those raised in the art by artisans of expertise.

In regards to an embodiment of the claimed invention, 1) a transgenic non-human animal other than mouse or goat, the specification provides guidance to make and use a transgenic mouse and goat. The specification does not teach a transgenic

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non-human animal of any species other than mouse or goat. For example, the specification provides no guidance to make a transgenic cow or non-human primate. Further, whereas the specification provides general guidance to make a transgenic pig comprising micropipetting a DNA solution containing a transgene construct into embryos recovered from pig oviduct and said embryos are transferred into a recipient pig, the specification does not provide specific guidance as to how to make and use said pig. The specification, therefore, does not provide sufficient guidance to make and use the full embodiment of the invention, any transgenic non-human animal.

In regards to an embodiment of the claimed invention, said invention encompasses 2) a transgene encoding any stearyl-CoA desaturase (SCD) wherein 3) said transgene is operably linked to an animal tissue specific promoter. The specification does not teach any transgenic non-human animal other than mouse or goat comprising a transgene encoding SCD. The specification does not teach any transgenic non-human animal comprising a transgene encoding any fatty acid desaturase other than SCD. Further, the specification does not teach any transgenic non-human animal comprising a transgene encoding SCD operably linked to any tissue specific promoter. At the time of the invention, the art of producing transgenic animals was (and remains) unpredictable. As the current state of the transgenic animal research stands, there are several significant limitations to the application of same methodology of making transgenic animals to different species. Longer gestation times, reduced litter sizes, number of fertilized eggs required for micro injection and relatively low efficiency of gene integration and method of introduction of transgenes are a few

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examples of such limitations. The variation in expression levels between different cell lines and species may be attributed to host genetic background, the site of chromosomal insertion and absence of specific transcription factors. Cameron (Cameron ER Molecular Biotechnology 7:253-276, 1997) noted, "Well regulated transgene expression is the key to successful transgenic work, but all too often experiments are blighted by poor levels or the complete absence of expression, as well as less common problems, such as leaky expression in non-targeted tissues. A feature common to many transgenic experiments is the unpredictable transgenic lines produced with the same construct frequently displaying different levels of expression. Further, expression levels do not correlate with the number of transgene copies integrated. Such copy-number-independent expression patterns emphasize the influence of surrounding chromatin on the transgene" (see page 256, section 4 on transgene regulation and expression).

Hammer et al. (Hammer RE et al. Cell 63 :1099-1112.1990) created both transgenic mice and rats expressing human HLA-b27 gene and beta-2 microglobulin. Although, both the transgenic animals bearing HLA-27 gene expressed the gene, transgenic mice did not show any HLA-2 associated disease whereas the transgenic rat demonstrated the most of the HLA-B27 related diseases (see lines 20-28 in col 2 of page 1099). This shows that the integration of a transgene into alternative species may result in a widely different phenotypic response even in animals of the same species. Additionally, promoters and enhancer elements may not function in all the species because they may require specific cellular factors. The specification does not provide

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any guidance as to whether a given promoter used for expressing an exogenous gene in one animal would have been functional in other animals and even if the promoter may have been active, whether the level of the transgenic product produced would have been sufficient to produce a certain phenotype. For example, the instant specification teaches generation of transgenic mice and goats comprising the same DNA construct expressing the rat stearyl CoA desaturase cDNA under control of the milk protein gene betalactoglobulin promoter. Progeny of primary transgenic mice and goats that were bred to non-transgenic control animals of the same genetic background produced milk samples that showed different fatty acid profiles. (pages 33-34, paragraphs 136-138) Whereas both transgenic lines showed an increased ratio of 18:1 versus 18:0 polyunsaturated fatty acid (PUFA) products of SCD, transgenic mice comprising the rat SCD gene showed a decreased ratio of 16:1 versus 16:0 monounsaturated fatty acids (MUFAs) product while transgenic goats comprising the same transgene produced milk that had an increased ratio of 16:1 versus 16:0 MUFA, indicating that the same transgene construct expressed in two different species of animals produces variant phenotypes. (pages 34-35, paragraphs 139-143) Therefore the art of transgenesis is unpredictable and a skilled artisan would require specific guidance to be enabled to make and use any transgenic non-human animal comprising a transgene encoding any fatty acid desaturase operably linked to any tissue specific promoter.

Further, whereas the specification provides guidance to make a transgenic mouse comprising a transgene encoding SCD operably linked to an epithelial tissue specific promoter, the specification does not teach a skilled artisan how to distinguish

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said transgenic mouse with a mouse comprising a transgene operably linked to a different tissue specific promoter and therefore does not provide guidance as to how to use said transgenic mouse. Without a phenotype by which to differentiate said transgenic mouse and in view of the unpredictability of transgenesis, a skilled artisan would not know how to use said transgenic mouse. Further, the specification does not provide guidance as to how to make and use a transgenic goat comprising a transgene encoding SCD operably linked to an epithelial tissue specific promoter. Therefore, in view of the intractable nature of transgenesis and the lack of guidance provided by the specification, a skilled artisan is not enabled to make and use any transgenic non-human animal comprising a transgene encoding any fatty acid desaturase operably linked to any tissue specific promoter.

In regards to an embodiment of the claimed invention, 4) a method for producing a non-human transgenic animal comprising a fatty acid desaturase transgene, the specification provides guidance to a skilled artisan to make a transgenic mouse or goat comprising a method microinjecting a SCD transgene into a single-celled mouse or goat embryo, and implanting said embryo into a recipient female mouse or goat wherein said mouse or goat embryo develops. The specification, however, does not enable a method for producing a transgenic animal comprising introducing a SCD transgene into a somatic cell, forming a genetically modified somatic cell, transferring the genetically modified nucleus of said somatic cell into a single-celled embryo, generating a genetically modified embryo and transferring said embryo into a recipient female wherein said embryo develops into a transgenic animal in said female.

At the time of the invention, the state of the art of somatic cell cloning was (and remains) unpredictable as well. Whereas the method of generating transgenic mice and other animal species using embryonic stem cells is well disclosed in the art, the state of the art of cloning using somatic cells is not. Wilmut et al (Nature 419:583-585, 2002) teach that studies in which somatic cell cloning has been used show that "only a small proportion of embryos reconstructed using adult or fetal somatic cells developed to become live young, typically between 0 and 4%," and that "somatic cell nuclear transfer is also associated with very high rates of fetal, perinatal and neonatal loss, and production of abnormal offspring." Similarly, Humpherys et al. (PNAS 99(20):12889-12894, 2002) teach that "the majority of cloned mammals derived by nuclear transfer die during gestation, display neonatal phenotypes resembling large offspring syndrome, often with respiratory and metabolic abnormalities, and have enlarged and dysfunctional placentas. (page 12889, paragraph 1). Therefore, due to the lack of guidance in the specification and the intractability of the art of somatic cell cloning, a skilled artisan is not enabled to make and use a method of producing a transgenic non-human animal comprising microinjecting a SCD transgene into a somatic cell of a non-human animal.

In regards to an embodiment of the claimed invention, 5) a method for producing a food product comprising harvesting or processing a food product from a non-human transgenic animal comprising a transgene encoding a fatty acid desaturase, the specification provides guidance to make and use milk from a transgenic mouse or goat comprising making a transgenic mouse or goat comprising a transgene encoding SCD operably linked to a mammary gland specific promoter wherein milk harvested or

processed from said mouse or goat has an altered fatty acid content as compared to non-transgenic controls. Whereas methods of harvesting or processing a food product from a non-human transgenic animal is known by a skilled artisan, said food product must inherently comprise an altered fatty acid content to be utilized for its intended use. However, at the time of the invention, the art of transgenic animals was unpredictable. The Mench JA (Transgenic Animals in Agriculture, pages 251-268, 1999) teaches "because there can be so much variation in the sites of gene insertion, the numbers of gene copies transferred, and gene expression, every transgenic animal produced using microinjection is (theoretically, at least) unique in terms of its phenotype." Wherein the intended use of the invention is production of food products that have lower levels of saturated fatty acids, in view of the unpredictability of the art of transgenesis and the lack of guidance from the specification, a skilled artisan could not predictably harvest or process any food having an altered fatty acid content from any transgenic non-human animal comprising a fatty acid transgene operably linked to any tissue specific promoter. Therefore, a skilled artisan is provided guidance to make, but not use, any food product from said transgenic non-human.

The instant specification teaches working examples wherein transgenic mice and goats are generated using a method wherein a DNA construct designed to express the rat SCD cDNA in the mammary gland under control of the milk protein gene beta-lactoglobulin promoter was microinjected into a pronuclei collected from females of the same species that were superovulated. Surviving zygotes were then transferred into the oviducts of recipient females and offspring were genotyped. Milk samples from

mouse and goat transgenic animals were collected and analyzed for fatty acid composition. The instant specification further teaches a transgenic mouse generated using a method wherein a DNA construct designed to express rat SCD cDNA in the intestine under control of the FABpi promoter was microinjected into pronuclei collected from superovulated females. Surviving zygotes were then transferred into the oviducts of recipient females and offspring were genotyped.

While the level of skill of an artisan practicing the claimed invention will be high, in view of the unpredictability of the state of the art, an artisan would require specific guidance to carry out the full breadth of the claimed invention. Finally, in view of the lack of guidance from the instant specification and the unpredictability of the art of generating transgenic animals, it would take an undue burden of experimentation for a skilled artisan to make and use, commiserate with the full scope of the claimed invention, any transgenic non-human animal comprising a transgene encoding any fatty acid desaturase, to make and use a transgenic mouse, goat, or pig comprising a transgene encoding any fatty acid desaturase operably linked to any tissue specific reporter, to make and use a transgenic goat comprising a transgene encoding SCD operably linked to an epithelial tissue specific promoter, or to use a transgenic mouse comprising a transgene encoding SCD operably linked to an epithelial tissue specific promoter.

Therefore, in view of the breadth of the claims and the lack of guidance provided by the specification as well as the unpredictability of the art, the claimed invention is not enabled for its full breadth and limiting the scope of the claimed invention to a

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transgenic mouse or goat whose somatic and germ cells comprise a nucleic acid sequence encoding stearoyl-CoA desaturase (SCD) operably linked to a mammary gland specific promoter wherein said transgene is expressed in the mammary gland of said mouse and goat and wherein milk of said mouse and goat contains said SCD transgene, a method for harvesting or processing said milk, and a method of producing said mouse and goat wherein stearoyl-CoA desaturase transgene is microinjected into a single celled mouse or goat embryo wherein mouse or goat embryo is transferred into a mouse or goat female for development is proper.

5. Claims 1-8 and 13-21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The invention of Claim(s) 1-8 and 13-21 encompasses

- 1) any transgenic non-human mammal other than mouse or goat
- 2) any fatty acid desaturase
- 3) any animal tissue specific promoter

These non-human transgenic animals of these claim(s) are broad in scope, being defined on the basis of their effect, and not on any specific structure. The specification broadly discloses a transgenic mouse and goat comprising a transgene encoding SCD operably linked to a mammary tissue specific promoter wherein said mouse and goat

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were produced by a method comprising microinjection of a DNA construct comprising the rat SCD transgene into one-cell fertilized mouse and goat zygotes, surgically transferring said zygotes into a recipient female mouse or goat wherein said embryo develops into a transgenic mouse or goat in said female wherein milk was harvested and processed from said transgenic mouse and goat and analyzed for fatty acid content.

In analyzing whether the written description requirement is met for gene claims, it is first determined whether a representative number of species have been described by their complete structure. In regards to 1) any transgenic animal comprising a transgene encoding any fatty acid desaturase, the genus encompasses a large number of species that would have different structures, particularly in view of the unpredictability of the art of transgenesis. The instant specification does not disclose the physical structure, function and utility of a sufficient number of transgenic non-human animals that could represent the broad genus claimed. The claimed genus, for example, would encompass a transgenic mouse, pig, and snake comprising a transgene encoding any fatty acid desaturase. Whereas the specification discloses a transgenic mouse and goat comprising a transgene encoding SCD, it is not sufficient to represent the structure of the entire genus claimed.

Regarding 2) any fatty acid desaturase, the genus would encompass fatty acid desaturase genes from any animal which again would have different nucleic acid and amino acid sequence structure and the sequence of rat gene disclosed in the specification would not be representative of the entire genus. Since it is not realistic to

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expect that "the complete structure" of any transgenic animal could be described, this requirement is interpreted to be whether phenotypic consequences or other characteristics of the animals resulting from altering the genotype have been described. In the instant case, the claimed invention encompasses any non-human animal comprising a fatty acid desaturase. Considering the fact that the claimed invention encompass transgenic animals and there is not description of the phenotype of any mammal other than mouse and goat, the phenotype(s) of the claimed animals can not be predicted because the art of making transgenic animals is highly unpredictable. Kappel et al. (Curr Opin Biotech 3 :548-553, 1992) teach that "while the investigator has the ability to target transgene expression to a large extent, there are inherent cellular mechanisms that may alter the pattern of gene expression. For example, DNA imprinting, resulting from differential CpG methylation, may affect transgene expression, dependin on the sex of the parent from which the gene was inherited. Alternatively, a detrimental transgene may undergo somatic deletion.

In regards to 3) a tissue specific promoter, the specification does not disclose the physical structure, function and utility of a transgenic non-human animal comprising a fatty acid desaturase operably linked to any tissue specific promoter. The claimed genus encompasses any tissue specific promoter such as epithelial, smooth muscle, cardiac muscle promoters. Whereas the specification discloses a transgenic mouse and goat comprising a transgene encoding SCD operably linked to a mammary tissue specific promoter, it is not sufficient to represent the structure of the entire genus claimed. For example, the specification describes a method to produce a transgenic

mouse comprising a transgene encoding SCD operably linked to an epithelial tissue specific promoter, the disclosure does not describe the complete structure, function or utility of said mouse. A skilled artisan could not envision, based on the description provided by the instant specification, the physical characteristics of said mouse such as PUFA content, MUFA content, epithelial cell appearance, etc.

Further, a skilled artisan could not envision the physical characteristics of a transgenic mouse comprising a transgene encoding SCD operably linked to any tissue specific promoters. Compounded with the intractable nature of transgenesis, the use of tissue specific promoters in transgenesis is also unpredictable. Cowan et al. (Xenotransplantation 10: 223-231, 2003) teach promoters of three human genes, ICAM-2, hCRPs, and PECAM-1, which are predominantly expressed in vascular endothelium in mice and pigs. When tissue specific expression was measured, it was found that whereas mice showed a distinct expression profile of the three human genes, the tissue expression profiles of the three human gene promoters were distinctly different in pigs. The authors concluded that "promoter performance in mice and pigs was not equivalent," and that "the weak expression driven by the human ICAM-2 promoter in pigs relative to mice suggests the need for additional regulatory elements to achieve species-specific gene expression in pigs. (page 223, paragraph 1) Therefore, in view of the unpredictability of promoters in the art of transgenesis, the working example provided in the specification does not allow a skilled artisan to envision the specific structure, function and utility of any transgenic non-human animal comprising any fatty acid desaturase linked to any tissue specific promoter.

Next then, it is determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics (i.e., other than nucleotide sequence), specific features and functional attributes that would distinguish different members of the claimed genus. In the instant case, the specification describes the physical characteristics of a transgenic mouse and goat comprising a transgene encoding SCD operably linked to a mammary tissue specific promoter. However, what would have been the result of expressing any fatty acid desaturase in any non-human animal could not be predicted. With the limited information disclosed in the specification, an artisan would have not been able to predict whether the animals would have had the same or different phenotypes compared to the transgenic mouse and goat. In order for a skilled artisan to be able to envision the genus of the claimed invention, the specific physical and chemical characteristics of the PUFA and MUFA compositions of each species would have to be described for a representative number of species in the genus due to the lack of description provided in the specification and unpredictability of the art of transgenic non-human animals. Therefore, the functional characteristics disclosed in the specification do not allow one of skill in the art to distinguish the different members of the very large genera from each other.

Applicant's attention is directed to *In re Shokal*, 113 USPQ 283 (CCPA 1957), wherein it is stated:

It appears to be well settled that a single species can rarely, if ever, afford sufficient support for a generic claim. *In re Soll*, 25 CCPA (Patents) 1309, 97 F2d 623, 38 USPQ 189; *In re Wahlforss*, 28 CCPA (Patents) 867, 117 F2d 270, 48 USPQ 397. The decisions do not however fix any definite number of species which will establish completion of a generic invention and it seems evident therefrom that such number will vary, depending on

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the circumstances of particular cases. Thus, in the case of small genus such as the halogens, consisting of four species, a reduction to practice of three, perhaps even two, might serve to complete the generic invention, while in the case of a genus comprising hundreds of species, a considerably larger number of reductions to practice would probably be necessary.

In conclusion, this limited information is not deemed sufficient to reasonably convey to one skilled in the art that Applicant is in possession of a transgenic non-human animal comprising a transgene encoding a fatty acid desaturase wherein said transgene comprises a coding sequence for a SCD operably linked to an animal tissue specific promoter, at the time the application was filed. Thus it is concluded that the written description requirement is not satisfied for the claimed genus.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

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6. Claims 1,2, 5, 13, and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Miyake et al. (J Biol Chem 276:23304-23311, 2001).

Claims 1 and 2 are directed to a transgenic non-human animal comprising a transgene encoding a fatty acid desaturase. Claim 5 is directed to said transgenic non-human animal wherein said transgene is chromasomally integrated. Claims 13 and 14 are directed to a method for producing a transgenic non-human animal comprising a fatty acid desaturase transgene comprising introducing a desaturase transgene into a single-celled embryo, forming a genetically modified embryo and transferring the genetically modified embryo into a recipient female of the same species wherein the genetically modified embryo develops into a transgenic non-human animal wherein said transgenic non-human animal is chosen from a mouse, rat, rabbit, pig, sheep, goat, poultry and cow.

Miyake et al. teach a non-human transgenic mouse comprising a chromasomally integrated transgene encoding 7 α -hydroxylase (CYP7A1), a fatty acid desaturase. Miyake et al. also teach a method for producing said mouse comprising generating a construct comprising a coding region for CYP7A1 under hepatic control wherein said construct is microinjected into single cell embryos of strain C57/Bl/6J mice and implanted into pseudopregnant female mice. Pups produced by this method were genotyped and shown to produce CYP7A1 mRNA produced from the transgene.

The art, teaching a transgenic non-human animal comprising a transgene encoding a fatty acid desaturase, meets all the limitations of claims 1, 2, 5, 13, and 14. The claims are therefore rejected for being anticipated by Miyake et al.

7. Claims 1-5, 13-15, 20 –21 are rejected under 35 U.S.C. 102(e) as being anticipated by Knutzon et al. (U.S. Patent No. 5,968,809 filed October 19, 1999).

Claims 1-5 are directed to a transgenic non-human animal comprising a transgene encoding a fatty acid desaturase wherein said animal is a mammal wherein said animal is an ungulate wherein said animal is poultry wherein said transgene is chromasomally integrated. Claims 13-15 are directed to a method for producing a transgenic non-human animal comprising a fatty acid transgene comprising introducing a desaturase gene into a single-celled embryo, transferring said embryo into a recipient female wherein said genetically modified embryo develops into a transgenic non-human animal wherein said method comprises a mammal, mouse, rat, rabbit, pig, sheep, goat, poultry or cow, wherein said transgene is expressed in mammary glands cells of said mammal. Claims 20-21 are directed to a method of producing a food product comprising harvesting or processing a food product from a transgenic non-human animal comprising a transgene encoding a fatty acid desaturase.

Knutzon et al. teach transgenic non-human animals comprising mice, rats, rabbits, chickens, quail, turkeys, bovines, sheep, pigs, goats, and yaks wherein said transgenic non-human animal comprises a transgene encoding a fatty acid desaturase such that animals express increased levels of desaturase. (column 15, lines 56-65) The authors further teach a method wherein a construct comprising a gene encoding the desaturase polypeptide is "introduced by microinjection of said construct into the

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pronuclei of a fertilized egg, or by transfection, retroviral infection or other techniques wherein the construct is introduced into a cell line which may form or be incorporated into an adult animal whereby the recombinant eggs or embryos are transferred to a surrogate mother." (column 17, lines 25-35) Progeny would then be genotyped for a marker gene. Knutzon et al. also teach expression of the desaturase transgene in mammary cells by using "specific regulatory sequences" such as those of bovine α -lactoglobulin, β -lactoglobulin or whey acidic protein such that production of PUFAs is obtainable from host milk. (column 17, line 54 to column 18, line 12)

Knutzon et al. teach transgenic non-human animals comprising mouse, rat, rabbit, pig, sheep, goat, poultry or cow wherein said animal comprises a transgene encoding a fatty acid desaturase wherein said transgene is chromasomally integrated wherein said animal is used in a method wherein a food product is harvested or processed from said animal. The disclosed invention of Knutzon et al. fully meets the limitations of claims 1-5, 13-15 and 20-21. The claims are therefore anticipated by the art and are rejected.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. Claims 1-8, 13-17, 20-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Knutzon et al. as applied to claims 1-8, 13-17, 20-21 above, and further in view of Ward et al; (Biochem Soc Trans 25(S673):145, 1997).

Claims 1-8, 13-17, 20-21 are directed to a non-human animal comprising a transgene encoding a fatty acid desaturase wherein said animal is a mammal, ungulate, or poultry wherein said transgene is chromosomally integrated and comprises a coding sequence for a SCD operably linked to an animal tissue specific promoter wherein said animal tissue specific promoter is a mammary specific promoter or an intestinal epithelium specific promoter, a method for producing said animal comprising introducing a desaturase transgene into a single-celled embryo, forming a genetically modified embryo and transferring said embryo into a recipient female of the same species wherein said embryo develops into a transgenic non-human animal, and method of producing a food product comprising harvesting or processing a food product from said animal.

Knutzon et al. teach transgenic non-human animals comprising mammal, mouse, rat, rabbit, pig, sheep, goat, poultry or cow wherein said transgenic non-human animal comprises a transgene encoding a fatty acid desaturase such that animals express increased levels of desaturase. (column 15, lines 56-65) The authors further teach a method wherein a construct comprising a gene encoding the desaturase polypeptide is "introduced by microinjection of said construct into the pronuclei of a fertilized egg, or by transfection, retroviral infection or other techniques wherein the construct is introduced

into a cell line which may form or be incorporated into an adult animal whereby the recombinant eggs or embryos are transferred to a surrogate mother.” (column 17, lines 25-35) Progeny would then be genotyped for a marker gene. Knutzon et al. also teach expression of the desaturase transgene in mammary cells by using “specific regulatory sequences” such as those of bovine α -lactoglobulin, β -lactoglobulin or whey acidic protein such that production of PUFAs is obtainable from host milk. (column 17, line 54 to column 18, line 12)

Ward et al. teach a method for increasing the proportion of monounsaturated fatty acids in ruminant carcass by “increasing the proportion of oleic acid in ovine tissue by manipulating the expression of the enzyme SCD.” (page 145, paragraph 1) The authors also recite literature that show that SCD homologues for human, rat, and mouse had been cloned and sequenced. The authors further teach the cloning of the ovine stearyl-CoA desaturase gene.

At the time of the invention, the SCD gene had been cloned and sequenced for human, rat, and mouse. It would have been obvious to a skilled artisan to modify the method of Knutzon et al. to generate transgenic non-human animals comprising a transgene encoding a fatty acid desaturase for the production of food products from said animals using a cloning method with the teachings of Ward et al. by expressing SCD in said transgenic non-human animals. Further, a skilled artisan would have expected a reasonable level of success because Knutzon et al. teach a transgenic non-human animal and a method for making said animal comprising introducing a transgene for a fatty acid desaturase into a transgenic non-human animal wherein said animal

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comprises an altered proportion of polyunsaturated and monounsaturated fatty acids, while Ward et al. teach a transgenic ovine comprising a transgene for SCD, a fatty acid desaturase, as a means for producing a transgenic ovine comprising an altered proportion of polyunsaturated and monounsaturated fatty acids.

A skilled artisan would have been motivated to modify the transgenic non-human animal taught by Knutzon et al. to express SCD as taught by Ward et al. because SCD reduces stearyl-CoA into a monounsaturated fatty acid which would alter the proportion of MUFAs and PUFAs in animal species used for food products, specifically ovine. Ward et al. teach that since MUFAs have the effect of lowering plasma LDL without the concomitant increase in HDL and meat products account for a quarter of fat intake of human diets, "it may be advantageous to increase the proportion of MUFAs in the ruminant carcass." (page 145, paragraph 1-2)

Conclusion

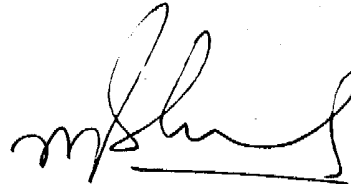
9. No claims are allowed.
10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Norma C Alonzo whose telephone number is 571-272-2910. The examiner can normally be reached on 8-5pm.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on 571-272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

NCA

A handwritten signature in black ink, appearing to read 'mshukla', with a horizontal line underneath.

RAM R. SHUKLA, PH.D.
PRIMARY EXAMINER